Laparoscopic versus open total mesorectal excision for rectal cancer (Review)

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ABSTRACT

Background
Because definitive long-term results are not yet available, the oncological safety of laparoscopic surgery for treatment of rectal cancer remains controversial. However, laparoscopic total mesorectal excision (LTME) for rectal cancer has been proposed to have several short- term advantages in comparison with open total mesorectal excision (OTME).

Objectives
To evaluate whether there are any relevant differences in safety and efficacy after elective LTME, for the resection of rectal cancer, compared with OTME.

Search strategy
We searched MEDLINE, EMBASE, Cochrane Central register of Controlled Trials (CENTRAL), and Current Contents from 1990 to December 2005. Searches were conducted using MESH terms: "laparoscopy", "minimally invasive","colorectal neoplasms". Furthermore we used the following text words: laparoscopy, surgical procedures, minimally invasive, rectal cancer, rectal carcinoma, rectal adenocarcinoma, rectal neoplasms, anterior resection, abdominoperineal resection, total mesorectal excision.

Selection criteria
We included randomised controlled trials (RCTs), controlled clinical trials and case series comparing LTME versus OTME. Furthermore case reports which describe LTME were also included.

Data collection and analysis
Two reviewers independently assessed study quality. All relevant studies have been categorized according to the evidence they provide according to the guidelines for "Levels of Evidence and Grades of Recommendation" supplied by the "Oxford Centre for Evidence-based Medicine". Disagreements were solved by discussion.

Main results
80 studies were identified of which 48 studies, representing 4224 patients, met the inclusion criteria. Methodological quality of most of the included studies was poor; three studies were grade 1b (individual randomised trial), 12 grade 2b (individual cohort study), 5 grade 3b (individual case-control study) and 28 grade 4 (case-series). As only one RCT described primary outcome, 3-year and 5-year disease-free survival rates, no meta-analyses could be performed. No significant differences in terms of disease-free survival rate, local recurrence rate, mortality, morbidity, anastomotic leakage, resection margins, or recovered lymph nodes were found. There is evidence that LTME results in less blood loss, quicker return to normal diet, less pain, less narcotic use and less immune response. It seems likely that LTME is associated with longer operative time and higher costs. No results of quality of life were reported.

Authors' conclusions
Based on evidence mainly from non-randomized studies, LTME appears to have clinically measurable short-term advantages in patients with primary resectable rectal cancer. The long-term impact on oncological endpoints awaits the findings from large on-going randomized trials.

PLAIN LANGUAGE SUMMARY

We have reviewed all studies that report on safety and efficacy after elective laparoscopic Total Mesorectal Excision (LTME) for the resection of rectal cancer. This review include 48 studies, identified from 80 references retrieved until December 2005. As only one RCT described primary outcome, 3-year and 5-year disease-free survival rates, no meta-analyses could be performed. No significant differences in terms of disease-free survival rate, local recurrence rate, mortality, morbidity, anastomotic leakage, resection margins, or recovered lymph nodes were found. There is evidence that LTME results in less blood loss, quicker return to normal diet, less pain, less narcotic use and less immune response. It seems likely that LTME is associated with longer operative time and higher costs. No results of quality of life were reported. The limited evidence suggests that LTME has clinically relevant short-term advantages in selected patients with rectal cancer.

BACKGROUND

Total mesorectal excision (TME) has become the surgical treatment of choice for rectal cancer. It achieves complete excision of the rectum together with its draining lymphatics, and results in low rates of recurrence (Heald 1986).

Laparoscopic and laparoscopic-assisted TME (LTME) offers several theoretical advantages over laparotomy. It may be associated with less blood loss, faster recovery, early feeding and a lower morbidity rate (Braga 2002; Pikarsky 2002). The magnified view of the pelvis afforded by the laparoscope may facilitate identification of the autonomic nerves and thus prevent unintentional injury.

However, these advantages of LTME are only beneficial to patients with rectal cancer when local recurrence and disease free survival rates of this technique is at least similar to that of open TME (OTME). LTME has been shown to achieve oncological resection equivalent to that of OTME (Breukink 2005 b; Kockerling 1998; Rullier 2003).

Because definitive long-term results are not yet available, oncological adequacy of LTME for treatment of rectal cancer remains unproven.

The lack of widespread use of LTME for rectal cancer may be related to the associated increase in operating time, cost and the relatively extensive learning curve (Leung 1999, Weeks 2002).

It is the purpose of this review to assess the safety and efficacy of laparoscopic TME for the resection of rectal cancer as compared with open TME.

OBJECTIVES

To evaluate whether there are any relevant differences in safety and efficacy after elective (LTME) for the resection of rectal cancer compared with open total mesorectal excision (OTME).

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised controlled trials (RCTs), controlled clinical trials, case series, or case reports which describe LTME will be considered for inclusion. Only clinical studies are included.

Types of participants

All patients with rectal cancer undergoing LTME.

Types of intervention

Laparoscopic or laparoscopic-assisted Total Mesorectal Excision. The anastomosis can either be performed intraperitoneally (i.e. 'double-stapled' colorectal anastomosis) or extraperitoneally (i.e. hand sewn or stapled colorectal anastomosis).

Types of outcome measures

The primary outcome was 3-year and 5-year disease-free survival rates.

Secondary outcomes of interest included:

- local recurrence
- mortality
- morbidity
- anastomotic leakage
- blood loss
- incidence of blood transfusions
- duration of surgery
- conversion rate
- adequacy of oncological resection; margins
- adequacy of oncological resection; lymph nodes removed
- gastrointestinal recovery rate
- postoperative pain, pain score
- postoperative pain, analgesia
- hospital stay
- quality of life
- cost
- immunologic response

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Colorectal Cancer Group methods used in reviews.

We have searched the following bibliographic databases in order to identify relevant primary studies: Cochrane Central register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and Current Contents from 1990 to December 2005. Searches have been carried out using medical subject headings (MeSH) and free text words. This search have been adapted for each database search:
- laparoscopy [MeSH],
- minimally invasive [MeSH]
- colorectal neoplasms [MeSH]
- laparoscopy [text]
- surgical procedures [text]
- minimally invasive [text])
- rectal cancer [text]
- rectal carcinoma [text]
- rectal adenocarcinoma [text]
- rectal neoplasms [text])
- anterior resection [text]
- abdominoperineal resection [text]
- total mesorectal excision).

The reference list of all relevant articles have been searched for further relevant studies. There was no language restriction. Only full, original articles from peer-reviewed journals have been included, no abstracts, to provide adequate detail on patient selection, allocation, study design, outcome, and measurement methods to allow an accurate, unbiased assessment and comparison of the study results.

METHODS OF THE REVIEW

All studies that meet the selection criteria have been assessed for methodological quality. This judgement has been performed by two reviewers (SB and JP); disagreements has been resolved by discussion. All relevant studies have been categorized according to the evidence they provide according to the guidelines for "Levels of Evidence and Grades of Recommendation" supplied by the "Oxford Centre for Evidence-based Medicine". (http://www.cebm.net/levels_of _evidence.asp).

1. A systematic review of randomised controlled trials (RCT) with homogeneity
1B. individual RCT (with narrow confidence interval)
1C. All or none case series
2A. systematic review of cohort with homogeneity
2B. individual cohort study (including low quality RCT; e.g. < 80 % follow-up)
2C. "outcomes" research
3A. systematic review of case-control studies (with homogeneity)
3B. individual case-control study
4. case-series (and poor quality cohort and case-control studies)
5. expert opinion without explicit critical appraisal, or based on physiology, bench research or 'first principles'.

DESCRIPTION OF STUDIES

We identified 80 studies of which 48 were included and 32 studies did not meet the inclusion criteria. 24 studies were excluded because they described the outcome of lapararoscopic surgery for colorectal cancer without sufficient description of the outcome of LTME. Five publications had to be excluded because the data were included in other publications (Barlehner 1998, Leung 1997; Leung 1999; Scheidbach 2001; Zhou 2003). One study was excluded because next to rectal adenocarcinoma different diagnoses were described (Iroatulam 1998). Another study was excluded because it described only one case (Kessler 2005) and one paper was excluded because the cadaver which was operated on had no rectal cancer (Decanini 1994).
The characteristics of the 48 included studies are summarised in the "Characteristics of includes studies" table. All 48 studies were reported as full papers and included a total of 4224 patients (range 5-308). 38 of the studies were prospective, three were retrospective. The remaining 7 studies did not report the way the data were obtained; prospective, or retrospectively. The included publications were 33 case series and 15 cohort studies.
The studies had quite similar exclusion criteria. The most common exclusion criteria were: T4 rectal cancer, rectal cancer recurrence, patients with synchronous or metachronous colorectal cancer, metastatic disease, emergency surgery, intestinal obstruction or perforation, contraindication for laparoscopy, no informed consent. The majority of the studies described the technique of laparoscopic TME. Perioperative treatment of patients was not described exactly in most of the trials. Exact data on the type of anaesthesia and analgesia were not given in many studies. In nearly all the studies several outcome parameters were reported. The most commonly assessed parameters were overall and disease-free survival rates, mortality, morbidity, anastomotic leakage, local recurrence, duration of surgery, adequacy of oncological resection (margins and number of lymph nodes removed), postoperative pain, gastrointestinal recovery rate, hospital stay and conversion. Not always the definition of conversion was described. The most common causes of conversion were tumour invasion of adjacent structures or bulky tumour adhesions and technical failure. Only few studies evaluated outcome measures like costs (Leung 2004 b) or immune response (Hu 2003Leung 2000 a) in detail. Only one of the 48 included studies described the surgical required experience to perform laparoscopic TME (Leung 2000 b).

METHODOLOGICAL QUALITY

As non-randomised studies were also included in the review and were the majority of the studies the usual criteria for assessing the quality of the included studies could not be used. As only one RCT described primary outcome, 3-year and 5-year disease-free survival rates, no meta-analyses could be performed (Leung 2004 b). Instead the studies were assessed according to the guidelines for "Levels of Evidence and Grades of Recommendation" supplied by the "Oxford Centre for Evidence-based Medicine". The reviewers assessed each study independently. Discrepancies were resolved by consensus.

The level of evidence of articles is low according to the chosen classification. Three of the 48 included studies were grade 1b (individual randomised trial), 12 grade 2b (individual cohort study), 5 grade 3b (individual case-control study) and 28 grade 4 (case-series).

The level 1b studies suffered from small sample sizes. Only one RCT included more than 100 patients (Leung 2004 b). Two of the three RCT reported on patients with rectosigmoid cancer (Leung 2000 a; Leung 2004 b) and only one study described exclusively the results of patients with rectal cancer (Zhou 2004).

The level 2b studies were generally of good quality. The largest level 2b study recruited 308 patients (Scheidbach 2002) and the smallest 70 patients (Yamamoto 2005).

No level 3a study was found by literature search and of the level 3b studies, the sample size ranged from 11 to 50. One paper included 11 patients in the LTME group and 22 in the open group (Pasupathy 2001).

The level 4 papers were largely of poor quality, with 14 of 28 studies not reporting study data in sufficient detail to assess the validity of the procedures (i.e. gender, exclusion criteria, tumour stage).

RESULTS

1. 3-year and 5-year disease-free survival rates

17 studies reported on long-term survival data of LTME. Only one RCT described the long-term outcome of sigmoid cancer and upper rectal cancer and found a 5 years disease-free survival rate of 75.3 % in the laparoscopic group and 78.3 % in the open group (p=0.45) (Leung 2004 b).

Data on long-term survival rates of LTME were given by 7 level 2b studies. Three of these papers showed a range of 67 -88 % of overall survival rate of 5 years (Barlehner 2005; Dulucq 2005; Poulin 2002). Two level 2b studies reported a 5-year disease-free survival rate ranging 63-75 % (Leroy 2004; Morino 2003). The only level 2b study containing data for APR and LAR separately, found a 2-year disease-free survival rate of 62.4 and 54.8 % respectively (Scheidbach 2002).

There was one level 3b study describing survival data with 92% of patients surviving 3 years in both the LTME as in the OTME group (Schwander 1999).

Seven level 4 studies described survival rate after LTME. Two of these 7 papers reported a 5 year disease-free survival rate ranging 62.5 -92.1% (Feliciotti 2003; Yamamoto 2002). The other 5 studies addressed to various degrees of long-term survival in patients after LTME.

2. local recurrence

31 studies reported data on local recurrence. Only one RCT examined data on local recurrence and found a rate of 6.6 % in the LTME group and 4.1% in the OTME group with a follow-up of 52.7 versus 49.2 months respectively (Leung 2004 b). After excluding one level 2b study, reporting a local recurrence rate of 33%, 8 level 2b studies gave data on local recurrence rates, with figures between 3.75 and 6.8%. All recurrence rates were reported between 16 and 45.7 months. The study reporting a recurrence rate of 33% included only patients who underwent an abdominoperineal resection. In this study the LTME group (n=28) was compared to the OTME group (n=61) and the same rate of local recurrence was found in the OTME group (33%) (Baker 2002).

Four level 3b studies described local recurrence data, ranging from 0 to 6%. No significant differences relating recurrence was found in these papers (Breukink 2005 a; Pasupathy 2001; Ramos 1997; Schwander 1999).

The 17 level 4 studies, showed a broad range of differences in local recurrence, with figures ranging from 0 to 24.1%. Five level 4 papers compared recurrence rate between laparoscopic and open surgery but none of them found a significant difference between the two groups.

3. mortality

Data on postoperative mortality was available from 37 studies; 3 of level 1b studies, 13 of level 2b, 2 of level 3b and 19 of level 4. One of the RCT reported a mortality rate of 2 % for the LTME group and 1 % for the OTME group (Leung 2004 b). One RCT reported a 0% death rate for both the LTME and OTME group but it included only 17 patients in both treatment arms (Leung 2000 a). The last RCT reported a mortality of 0 % for both groups (Zhou 2004).

Of the level 2b studies perioperative death rates varied between 0 % and 2.5%. The two level 3b studies reporting on mortality, described both a 0% death rate in both groups (Breukink 2005 a; Pasupathy 2001). Level 4 studies showed a broad range of mortality, ranging from 0 to 25 %. The 25 % mortality rate reported by one case serie can be explained by the fact that this study included only 4 patients of whom one patient died after a perforated duodenal ulcer (Larach 1993).

4. morbidity

Morbidity was reported in 36 studies. All the three RCT reported on morbidity, with a range of 6.1 to 29 % for the LTME group

and a range of 12.4 to 35 for the OTME group. Only one RCT found a significant difference in morbidity between the LTME and OTME group (6.1% versus 12.4%; p= 0.016) (Zhou 2004). The other two RCTs did not report on whether a statistical test of significance was performed.

Of the level 2b studies 9 studies reported on morbidity, with rates between 20% and 37.6%. Morbidity rates were available of four level 3b studies. One study did not find any significant difference between the laparoscopic and open procedure (p=0.26), but it included only 45 patients in both arms (Breukink 2005 a). The other three level 3b papers did not report statistical analysis of the two procedures.

Of the level 4 studies, a total of 20 papers presented data on morbidity, with a wide range of 0 to 76%. The highest rate of 76% was found by Fleshman et al. who included only abdominal perineal resections (Fleshman 1999). In contrast to the level 4 study that reported a morbidity rate of 0%, which described only data of patients who underwent low anterior resection (Hu 2003). Of the 20 level 4b studies, there were 10 studies comparing data of LTME group with an open control group. Two of those 10 studies found signficant less morbidity in the LTME group (Anthuber 2003, Wu 2004), one did not find a difference between the two groups (Vithiananthan 2001) and the remaining 7 studies provided no statistical comparison between the two procedures.

5. anastomotic leakage

29 trials gave data concerning anastomotic leakage. Two of the RCTs reported data on anastomotic leakage, but both did not find any significant difference between the two groups (Leung 2004 b; Zhou 2004). A range of 0.5 to 1.2% of anastomotic leakage was found in the two RCTs.

Nine level 2b studies described anastomotic leakage rates, ranging from 3 to 17%. The paper that described a leakage rate of 17% reported on 102 patients who underwent LTME (Leroy 2004).

Of the two level 3b studies reporting on anastomotic leakage none found any significant difference between the laparoscopic and open approach (Breukink 2005 a; Schwander 1999). 16 level 4 studies reported on anastomotic leakage with a range of 0 to 25%. The paper that described a leakage rate of 25 % reported the results of 8 male patients who underwent a laparoscopic low anterior resection (Chen 2002).

6. blood loss

Data on blood loss was given by 17 studies. All three RCTs reported on blood loss and two of them found significantly less blood loss in the LTME group compared to the OTME group (Leung 2004 b, Zhou 2004). The other RCT did find less blood loss in the laparoscopic group (103 versus 141 ml) but the difference did not reach significance, probably due to the limited patients (n=17) (Leung 2000 a).

Three level 2b studies, 1 level 3b and 10 level 4 studies reported on blood loss. Of the level 2b studies a range of 56 to 436 ml in the LTME group was reported (Kockerling 2000; Law 2004; Yamamoto 2005). The only level 3b study, reporting on blood loss, found less blood loss in the LTME group compared to the OTME group (250 versus 1000 ml; p<0.001) (Breukink 2005 a). Three of the level 4 studies compared data between the two groups; 2 of them found significantly less blood loss in the LTME group (Leung 2000 b; Wu 2004).

7. incidence of blood transfusions

Data on blood transfusions was reported by 10 studies. The only RCT giving data on blood transfusions found no significant difference between the two treatment arms (6% versus 12%; p=n.s) (Leung 2000 a).

Four level 2b studies reported on blood transfusion; the range varied between 1 and 6% (Barlehner 2005; Dulucq 2005; Law 2004; Morino 2003). The single level 3b study that examined blood transfusion found significantly less transfusions in the laparoscopic group (1.2 versus 2.4%, p=0.017) (Schwander 1999). The 4 level 4 studies assessing blood transfusions, described a broad range of blood transfusions given to patients who were operated laparoscopically (2-25%) (Anthuber 2003,Bruch 1997; Rullier 2003; Wu 1997).

8. duration of surgery

Operative time was estimated in 38 studies. Of the three RCTs that measured this variable, two of them found a longer operative time in the laparoscopic group compared to the open group (Leung 2000 a; Leung 2004 b); the other RCT was close to significance (p=0.051) (Zhou 2004).

11 level 2b studies showed a range of 138 to 267 minutes of operative time in the laparoscopic group. 4 level 3b studies compared the duration of surgery between the two groups. Only one of them found a significant difference between the two groups (281 versus 209 minutes; p=0.004) (Schwander 1999). Of the 20 level 4 studies, there were 10 studies with an open control group. Six of them found a shorter surgical time for the OTME group.

9. conversion rate

There were 36 studies assessing conversion rate. The single RCT giving data of conversion found a rate of 23.2% (Leung 2004 b). Twelve level 2b studies measured the conversion rate in the laparoscopic group. The variability between these studies was quite high, showing a range of 0 to 18.25%. Of the level 3b studies, 4 reported on conversion rates, which varied between 0 and 10% (Breukink 2005 a; Breukink 2005 b; Ramos 1997; Schwander 1999). Of the 19 level 4 studies, again, the conversion rates varies widely, from 0% to 33%. For most studies surgeons experience was not clearly stated.

10. adequacy of oncological resection; margins

There were 16 studies reporting results of resection margins. None of the RCT discussed this items. Two level 2b studies reported data on surgical margins. Both did not find positive resection margins (Leroy 2004; Morino 2003).

Of the 2 level 3b studies that reported results of resection margins, one did not find positive margins in both groups (Schwander 1999). The other study assessed the circumferential resection

margin and did not find a significant difference between the two groups (Breukink 2005 b).
Of the 12 level 4 studies reporting on resection margins, 7 studies reported data with an open control group. One of these 7 papers did not find a significant difference between laparoscopic and open surgery (Leung 2000 b). The other six studies did not report on whether a statistical test of significance was performed.

11. adequacy of oncological resection; lymph nodes removed
There were 32 studies reporting data on adequacy of lymph node dissection; 1 level 1b, 9 level 2b, 4 level 3b and 18 level 4 studies. The single RCT that has measured this variable found no differences between the two groups (11.1 versus 12.1, p=0.18) (Leung 2004 b). Of the level 2b studies, the number of lymph nodes resected varied between 6 and 25. None of the 4 level 3b studies found a significant difference between the open and laparoscopic approach (Breukink 2005 a; Breukink 2005 b; Ramos 1997; Schwander 1999). Of the level 4 studies with an open control group only one paper found significant less lymph nodes in the laparoscopic group (15 vs 22, p<0,001) (Anthuber 2003).

12. gastrointestinal recovery rate
29 studies examined gastrointestinal recovery rate, defined by resumption of solid food expressed in days. All three RCTs measured this item and only one RCT found that patients undergoing laparoscopic surgery began solid food intake significantly sooner than patients in the open group (4.2 versus 4.9; p<0.001) (Leung 2004 b). 6 level 2b studies reported on gastrointestinal recovery rates, which varies between 2 and 4.9 days. Of the four level 3b studies, 3 found that patients who underwent LTME significantly returned to a normal diet than patients who has been operated laparoscopically (Breukink 2005 a; Ramos 1997; Schwander 1999). Of the 16 level 4 studies, 10 reported data with an control group of patients who underwent open surgery. 4 of them found a quicker return to normal diet in the laparoscopic group (Leung 2000 b; Seow-Choen 1997; Tate 1993; Wu 2004). Two found no significant difference between the two groups (Goh 1997; Vithiananthan 2001) and 4 did not report statistical analysis of the two procedures (Darzi 1995, Fleshman 1999; Hartley 2001; Hu 2003).

13. postoperative pain, pain score
Only 2 trials reported data on postoperative pain score (Leung 2000 a; Leung 2004 b). Both were RCTs and used a visual analog scale to objectivate postoperative pain. The RCT with limited patients (n=17) did not find a significant difference between the two groups (5.5.vs 6.25; p=n.s.) (Leung 2000 a). The other RCT reported significant less pain in the laparoscopic group (4.6 vs 5.4; p=0.003) (Leung 2004 b).

14. postoperative pain, analgesia
Only 13 papers measured anlagesic use. Either it was assessed by the total number of doses analgesia given or by the total number of days during which analgesia was required. Two of the 3 RCTs did not find a significant difference between laparoscopic and open approach though a trend for less analgesia was seen for the laparoscopic group (Leung 2000 a; Zhou 2004). One RCT, measuring the number of injections, found that in the laparoscopic group 3 injections were needed versus 6 injections in the open group (p=n.s.) (Leung 2000 a). The other RCT, reporting no difference between the two groups, measured the use of analgesia in days, 3.9 vs 4.1; p=0.225 (Zhou 2004). The RCT which did find a significant difference between the two groups included the largest sample size of 200 patients in each group (Leung 2000 a). They reported that the laparoscopic group needed 4.5 injections and the open group 6.9 (p<0.001).
Two level 2b studies reported on analgesic use, but different regimens were followed, therefore they were difficult to compare (Morino 2003; Schiedeck 2000). Of the level 3b studies, 3 reported data on analgesia use. Two of the three found that the laparoscopic group used significantly less analgesia (Pasupathy 2001; Ramos 1997). The other one reported less analgesia in the laparoscopic group but did not find a significant difference (Schwander 1999).
Of level 4 studies 5 described data on postoperative analgesia. Three papers used an open control group. Two of these three studies found a significant less analgesia use in the laparoscopic group (Leung 2000 b, Tate 1993).

15. hospital stay
39 studies reported data on hospital stay. Two of the three RCTs reported that patients undergoing laparoscopic surgery were significantly more likely to be discharged earlier from the hospital than patients undergoing open surgery (Leung 2004 b; Zhou 2004). The other RCT did not find any difference between the two groups (Leung 2000 a).
9 level 2b were found reporting on hospital stay. One level 2b study reported a significant shorter postoperative hospital stay in the laparoscopic arm (13 versus 18 days; p=0.008) (Baker 2002). Hospital stay was assessed by 4 level 3b studies. Three of the 4 showed a significantly shorter hospital stay for patients undergoing LTME compared to OTME (Breukink 2005 a, Ramos 1997; Schwander 1999).
Of the 23 level 4 studies, the variability of hospital stay was quite high with a range reaching from 5 to 18.3 days in the laparoscopic groups and from 5.5 to 25 days in the open groups of the studies.

16. quality of life
There were no studies reporting on quality of life.

17. cost
Only one paper compared the direct cost of operation between LTME and OTME. The only study that reported on this variable, was a RCT and found that the cost of LTME was US$ 2100 more expensive than OTME (Leung 2004 b).

18. immunologic response
Two papers addressed the issue of tissue trauma and immune response to laparoscopic surgery. One RCT included only 17 patients in each group (Leung 2000 a) and assessed Interleukin-1, interleukin-6, C-reactive protein levels and tumour necrosis fac-

tor-(alpha). The levels of Interleukin-1, interleukin-6, C-reactive protein were significantly less in the laparoscopic group. No difference was found between the two groups in levels of tumour necrosis factor-(alpha).

The other paper was a level 4 study comparing 20 patients who underwent a laparoscopic low anterior resection with 25 patients who underwent an open low anterior resection (Hu 2003). In this study Interleukin-2, interleukin-6, tumour necrosis factor-(alpha), CD3+, DC56+, T lymphocyte count, CD3-, CD56+ natural killer cell (NK) count and immunoglobulin (IgG/IgM/IgA) was assessed and no significant differences were found between the two groups.

DISCUSSION

Fifteen years after the first report of laparoscopic surgery for colorectal disease (Jacobs 1991), the level of evidence of studies concerning the safety and efficacy of LTME is low. Since 1990 48 studies have been published to answer the question whether LTME is more safe and efficient than OTME. As there are only 3 RCTs, the inclusion criteria of this review were modified to enable the inclusion of more studies regardless their level of evidence. Of the 3 RCTs two reported on results of patients undergoing sigmoidectomy of high anterior resection for tumours in the sigmoid of upper rectum (Leung 2000 a; Leung 2004 b) and one of them included only 17 patients in each arm (Leung 2000 a). Only one study described exclusively the results of patients with rectal cancer with inclusion of 82 patients in LTME group and 89 patients in the OTME-group (Zhou 2004).

The majority of papers were level 4 studies (58%) and are feasibility studies. Nonrandomized cohortstudies (level 2b) and case-control studies (level 3b) were spare. The assessment of various important variables was limited by missing data and by heterogeneity of protocols resulting in a lack of reliable consistent evidence. Furthermore, the study samples included in this review are relatively small (5 to 308 patients) and none of the included studies have made an estimate of what sample size is needed to detect differences based on a well defined primary outcome between LTME and OTME. The results of this review are therefore to be interpreted with care. Despite these shortcomings, the included studies were useful in providing information on safety and efficacy of LTME.

The definitive criterion for the evaluation of LTME as an established therapeutic technique in curative rectal surgery is the long-term outcome, particularly the 5 year and 3 year disease-free survival and local recurrence rates. This review shows no indication of poorer long-term outcome or higher local recurrence rate of LTME compared with OTME. In the included studies the median follow-up period varies considerably between the studies and groups which may have influenced the results.

In this review no significant difference between LTME and OTME in terms of perioperative death rates were found. Overall, no evident difference in morbidity between the two groups was found, only in one RCT a significant lower morbidity rate was found in the laparoscopic group (Zhou 2004). The studies with an open control group showed a trend of lower morbidity for the LTME group although most of these studies did not report whether a statistical test of significance was performed. There was no difference in anastomotic leakage between the LTME and OTME groups.

It can be concluded from the studies reviewed that blood loss is significantly less in the laparoscopic group. However, not evident less blood transfusions were given in the laparoscopic group, although this item was only measured in 10 studies of which one was a RCT with 17 patients included (Leung 2000 a). One distinct disadvantage of LTME is the relatively longer operative time. Due to the lack of data, it was not possible to make a difference between LAR and APR. Besides, the included studies often described operative time of mixed patients undergoing low anterior resection or abdominoperineal resection.

In this review a high variability of conversion rate was seen (0-33%). The lack of consensus in the definition used by different studies made results of this item difficult to interpret. Furthermore, the required experience of surgeons was often not mentioned. Heterogeneity is magnified by differences in surgeon skills, experience and patient selection, therefore, the results may not be applicable to a general daily colorectal practice.

In this review, the surgical margins and number of removed ymph nodes of the laparoscopic group was equal to those obtained from the open group. The postoperative period of LTME offers the most benefits compared to OTME. There is evidence that LTME results in an earlier return of normal diet, less pain, less narcotic use and shorter hospital stay.

Since one of the main benefits for laparoscopic surgery concern the reduction of patient discomfort and inconvenience, it is surprising that quality-of-life measure were not used in the included studies to assess patient perception an outcomes. It seems likely that the operative costs of LTME are higher than OTME, although the evidence base is too narrow and more RCTs are required to answer this question as only one RCT has assessed this variable yet (Leung 2004 b).

Finally, there is some possibility that immune response to LTME is less than to OTME although the evidence base is thin in this regard as there are only 2 studies reporting on this item. One RCT found significantly less immune response after LTME compared with OTME and the other paper (Leung 2000 a), a level 4 study, did not find any differences between the two groups (Hu 2003).

The studies included in this review do not allow firm conclusions as to the question of whether the safety and efficacy of LTME is equal or superior to OTME. But this review suggests that LTME has clinically relevant short-term

advantages in selected patients with rectal cancer. This is in accordance with results of laparoscopic colon surgery. A meta-anlaysis comparing short-term results of laparoscopic and open colon resection under traditional perioperative treatment shows that la-

pararoscopic colonic resection has clinically relevant advantages in selected patients (Schwenk 2005). Regarding LTME, good quality randomised controlled trials comparing short-term outcome of LTME with accelerated multimodal rehabilitation programmes are needed.

To evaluate long-term oncological outcome of LTME, follow-up should be at least 5 years and besides local recurrence rates outcome should include quality of life. A meta-analysis of four trials randomizing patients with colonic cancer to either laparoscopically assisted or open colectomy (COST trial, Barcelona trial, CLASSIC trial and COLOR trial (COLOR 1)) showed that laparoscopically assisted colectomy for cancer is oncologically safe (Bonjer 2005). Oncologic long-term data of LTME are eagerly awaited from studies such as the CLASSIC trial (Guillou 2005). Furthermore, the ongoing COLOR 2-trial, a multicenter, randomized clinical trial, assessing the outcome of patients undergoing laparoscopic resection of rectal cancer, should provide more information on the suitability of LTME for rectal cancer (COLOR 2).

AUTHORS' CONCLUSIONS

Implications for practice

The studies included in this review do not allow firm conclusions as to the question of whether the safety and efficacy of LTME is equal or superior to OTME. Based on evidence mainly from non-randomized studies, LTME appears to have clinically measurable short-term advantages in patients with primary resectable rectal cancer. The long-term impact on oncological endpoints awaits the findings from large on-going randomized trials.

Implications for research

Good quality randomised controlled trials comparing short-term outcome of LTME with accelerated multimodal rehabilitation programmes are needed. To evaluate long-term outcome of LTME versus OTME follow-up should be at least 5 years. Besides local recurrence rates outcome should include quality of life.

POTENTIAL CONFLICT OF INTEREST

None known.

SOURCES OF SUPPORT

External sources of support

- No sources of support supplied

Internal sources of support

- No sources of support supplied

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Anthuber 2003**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 101 vs 334 Gender (%): male 58 vs 71; female: 42 vs 29 Inclusion: primary rectal cancer Exclusion: cT4 rectal cancer, rectal cancer recurrence, low transanally resectable tumours of early stage, patients with synchronous colorectal cancers or metachronous rectal cancer, emergency cases Tumour stage (%) UICC I 41 vs 22, II 18 vs 23 III 20 vs 29, IV 21 vs 26 Distance from anal verge (%): 16-12 cm = 25, 8-12 cm = 39, 0-8 =36
Interventions	laparoscopy vs open LAR (%): 77 vs 75 APR (%): 23 vs 25
Outcomes	mortality (%): 0 vs 1 (p=0.175) morbidity (%): 11 vs 25 (p=0) anastomotic leakage (%): 9 vs 7 (p=0.739) duration of surgery (min): 218 vs 218 (p=0.91) incidence of blood transfusions: 4 vs 28 (p=0) adequacy of oncological resection; lymph nodes removed: 15 vs 22 (p<0.001) hospital stay (days): 14 vs 20 (p=0)
Notes	conversions (%): 11 follow-up: no data given surgeons experience required: The choice of surgical technique in the individual patient was left to the responsible surgeon and was basically guided by gender, BMI, tumour location, and tumour size
Allocation concealment	D – Not used

Study	**Baker 2002**
Methods	Individual retrospective cohort study (level of evidence 2b) Retrospective
Participants	n = 28 vs 61 Gender: no data given Inclusion: all abdominoperineal resections commenced laparoscopically

Characteristics of included studies (*Continued*)

	Exclusion: no data given Tumour stage (%): UICC I 11 vs 13, II 31 vs 37, III 54 vs 41, IV 4 vs 9
Interventions	laparoscopy vs open APR (%): 100
Outcomes	mortality: 1 vs 2 local recurrence (%): 33 vs 33 adequacy of oncological resection; margins (%): 4 vs 18 (p=0.095) adequacy of oncological resection; lymph nodes removed: 6 vs 5 (p=n.s.) hospital stay (days): 13 vs 18 (p=0.008)
Notes	conversion (%): 8 follow-up: 36 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Barlehner 2005**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 194 Gender (%): male 64, female 36 Inclusion: no data given Exclusion: no data given Tumour stage UICC (%): I 25, II 27, III 31, IV 17 Distance from anal verge (%): 12-18 cm = 23; 7-12 cm = 44; 0-6 cm = 33
Interventions	only laparoscopy LAR (%): 92 APR (%): 8
Outcomes	5-year survival rate (%): 88 3-year survival rate (%): 91 mortality (%): 0 morbidity (%): 20 anastomotic leakage (%): 14 incidence of blood transfusion (%): 1 duration of surgery (min): 174 adequacy of oncological resection; lymph noded removed: 25 local recurrence (%): 4
Notes	conversion (%): 1 follow-up: 46 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Bokey 1997**
Methods	Case-series (level of evidence 4) prospective
Participants	n = 10 Gender: no data given

Characteristics of included studies (*Continued*)

	Inclusion: no data given Exclusion: no data given Tumour stage: no data given Distance from anal verge: no data given
Interventions	only laparoscopy LAR (%): 2 APR (%): 8
Outcomes	local recurrence (%): 0 duration of surgery (min): 342 adequacy of oncological resection; lymph nodes removed: 10 hospital stay (days): 16
Notes	follow up: 29 months
Allocation concealment	D – Not used

Study	**Bretagnol 2005**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 144 Gender (%): male: 61, female: 39 Inclusion: no data given Exclusion: T4 rectal cancer, synchronous resectable metastases, associated disease needing extensive colectomy Tumor stage UICC (%): I 4, II 13, III 83, IV 0 Distance from anal verge (%): 6-12 cm = 48, 0-6 cm = 52
Interventions	only laparoscopy LAR (%): 100
Outcomes	3-year disease-free survival rate (%): 77 mortality (%): 1 morbidity (%): 34 anastomotic leakage (%): 23 local recurrence (%): 1,4 adequacy of oncological resection: margins: distal = 3; circumferential = 9 adequacy of oncological resection; lymph nodes removed: 10
Notes	conversion (%): 14 follow-up: 18 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Breukink 2005 a**
Methods	Individual case-control study (level of evidence 3b) Prospective
Participants	n = 41 Gender (%): male: 61 vs 56, female: 39 vs 44 Inclusion: primary rectal cancer Exclusion: advanced T3 or T4 rectal cancer, previous transanal endoscopic microsurgery Tumour stage UICC (%): I 29, II 24, III 40, IV 7 Distance from anal verge (%):

Characteristics of included studies (*Continued*)

	> 12 cm = 29, 7-12 cm= 47, 0-6 cm = 24
Interventions	laparoscopy vs open LAR (%): 76 APR (%): 24
Outcomes	mortality (%): 0 vs 2 (p = n.s.) morbidity (%): 37 vs 51 (p = 0.26) anastomotic leakage (%): 8 vs 14 (p = n.s.) local recurrence (%): 0 vs 0 reoperation (%): 0 vs 5 blood loss (ml): 250 vs1000 (p<0.001) duration of sugery (min): 200 vs 180 (p=0.059) adequacy of oncologic resecton; margins (%): 7 vs 12 (p=n.s.) adequacy of oncological resection; lymph nodes removed: 8 vs 8 gastrointestinal recovery rate (days): 3 vs 6 (p=0.046) hospital stay (days): 12 vs 19 (p=0.007)
Notes	conversion (%): 10 follow-up: 14 months surgeons experience required: "experienced laparoscopic colorectal surgeons trained in TME surgery"
Allocation concealment	D – Not used

Study	**Breukink 2005 b**
Methods	Individual case-control study (level of evidence 3b) Prospective
Participants	n = 25 Gender (%): male 64, female 36 Inclusion: primary rectal cancer Exclusion: conversion Tumour stage UICC (%): no data given
Interventions	laparoscopy vs open LAR(%): 46 APR (%): 54
Outcomes	adequacy of oncological resection; circumferential resection margins (%): 12 vs 4 (p=n.s.) adequacy of oncological resections; lymph nodes removed: 11 vs 11 (p=n.s.)
Notes	conversion (%): 0 follow-up: no data given surgeons experience required: "experienced laparoscopic colorectal surgeons trained in TME surgery"
Allocation concealment	D – Not used

Study	**Bruch 1997**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 20 Gender (%): no data given Inclusion: no data given Exclusion: T4, rectal carcinoma, abdominal aortic aneurysm, synchronous colon cancer Tumour stage UICC (%): no data given Distance from anal verge (%):

Characteristics of included studies (*Continued*)

	no data given
Interventions	only laparoscopy LAR (%): 30 APR (%): 70
Outcomes	local recurrence (%): 5 incidence of blood transfusions: 2 duration of surgery (min): 315 adequacy of oncological resection: lymph nodes removed: 12 hospital stay (days): 16
Notes	conversion (%): 10 follow-up: 46 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Chen 2002**
Methods	Case-series (level of evidence 4)
Participants	n = 8 Gender (%): male 100 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 50, II 25, III 25, IV 0 Distance from anal verge (%): > 7 cm = 25, < 7 cm = 75
Interventions	only laparoscopy LAR (%): 100
Outcomes	mortality (%): 0 morbidity (%): 25 anastomotic leakage (%): 25 reoperation (%): 0 local recurrence (%): 0 blood loss (ml): 250 duration of surgery (min): 210 hospital stay (days): 13
Notes	conversion (%): no data given follow-up: 14 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Chung 2001**
Methods	Case-series (level of evidence 4)
Participants	n = 5 Gender (%): male 60, female 40 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 0, II 3, III 2, IV 0 Distance from anal verge: mean 7 cm

Characteristics of included studies (*Continued*)

Interventions	only laparoscopy LAR (%):100
Outcomes	mortality (%): 0 anastomotic leakage (%): 0 local recurrence (%): 0 duration of surgery (min): 208 blood loss (ml): 158 adequacy of oncological resection; margins (%):0 hospital stay (days): 10.6
Notes	conversion (%): no data given follow-up: 13 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Darzi 1995**
Methods	Case-series (level of evidence 4)
Participants	n = 12 vs 16 Gender (%): male 25 vs 31, female 75 vs 69 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 8 vs 19, II 33 vs 56, III 59 vs 25 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open APR (%): 100
Outcomes	mortality (%): 8 vs 25 morbidity (%): 33 vs 56 anastomotic leakage (%): 0 vs 0 reoperation (%): 8 duration of surgery (min): 195 vs104 adequacy of oncological resection; margins (%): 0 vs 2 adequacy of oncological resection; lymph nodes removed: 9.5 vs 6 gastrointestinal recovery rate for flatus (days): 3.2 vs 5.9 hospital stay (days): 11 vs 17.5
Notes	conversion (%): 0 follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Delgado 2004**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 220 Gender (%): male 66, female 34 Inclusion: rectal cancer Exclusion: intestinal occlusion, patients with anesthesic contraindication for pneumoperitoneum, patients who did not consent to inclusion after having been fully informed Tumour stage UICC (%): I 17, II 34, III 26, IV 19, in 4 % no tumour was found

Characteristics of included studies (*Continued*)

	Distance from anal verge (%): 12-15 cm =29, 7-12 = 31, < 7 = 40
Interventions	only laparoscopy LAR (%): 80 APR (%): 19 palliative stoma (%): 1
Outcomes	mortality (%): 1,3 morbidity (%): 26 anastomotic leakage (%): 7 local recurrence (%): 5,4 duration of surgery (min): 179 adequacy of oncological resection; lymph node removed: 14 gastrointestinal recovery rate (hours): 48 hospital stay (days): 6,8
Notes	conversion (%): 20 follow-up: 18 months surgeons experience required: "surgeons who have wide experience in colon surgery by laparoscopy"
Allocation concealment	D – Not used

Study	**Dulucq 2005**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 218 Gender (%): male 56, female 44 Inclusion: primary rectal cancer with lowest margin of tumour located 2 cm above the dentate line Exclusion: patients who were admitted due to emergency situations, distance metastases, patients with contraindication for laparoscopy, patients who underwent APR Tumour stage UICC (%): I 10,6, II 28,4, III 54,6, IV 6,4 Distance from anal verge (%): 11-15 cm = 35, 6-10 = 45, 0-5 = 20
Interventions	only laparoscopy LAR (%): 100
Outcomes	overall survival rate at 10 years (%) : 53,5 overall survival rate at 5 years (%): 67 mortality (%): 1 morbidity (%): 25,6 anastomotic leakage (%): 10,5 local recurrence (%): 6,8 duration of surgery (min): 138 blood loss (ml): 120 incidence of blood transfusion (%): 6 adequacy of oncological resection; lymph node removed: 25 gastrointestinal recovery rate (days): 3 hospital stay (days): 6
Notes	conversion (%): 12 follow-up: 57 months surgeons experience required: no data given

Characteristics of included studies (*Continued*)

Allocation concealment	D – Not used

Study	**Feliciotti 2003**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 81 vs 43 Gender (%): male 55 vs 53, female 45 vs 47 Inclusion: primary rectal cancer Exclusion: T1N0 rectal cancer, patients with rectal cancer who underwent local excision, emergency surgery Tumour stage UICC (%): I 35,4 vs 35,2, II 32,3 vs 32,4, III 32,3 vs 32,4, IV 0 vs 0 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%): 74 vs 63 APR (%): 26 vs 37
Outcomes	5-years disease-free survival rate: 62,5 vs 60,6 (p=0.623) mortality (%): 0 vs 0 (p=n.s.) anastomotic leakage (%): 13,5 vs 18,5 local recurrence (%): 20,8 vs 18,2 (p=0.687) adequacy of oncological resection; lymph node removed: 10,3 vs 9,8 (p=0.63)
Notes	conversion (%): 12,3 follow-up: 43,8 months surgeons experience required: no data given The treatment method (laparoscopic or open) was not randomized, but chosen by the patients without any pressure from the surgeon based on the stage of the disease.
Allocation concealment	D – Not used

Study	**Fleshman 1999**
Methods	Case-series (level of evidence 4) Retrospective
Participants	n = 42 vs 152 Gender (%): male 48 vs 43, female 52 vs 57 Inclusion: patients undergoing APR (open or laparoscopic) for rectal cancer Exclusion: no data given Tumour stage UICC (%): I 18 vs 26, II 24 vs 33, III 43 vs 32, IV 15 vs 9 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open APR (%): 100
Outcomes	overall survival rate at 5 years (%): 54 vs 60 (p=n.s.) mortality (%): 0 vs 0 morbidity (%): 76 vs 50 local recurrence (%): 21,4 vs 17 (p=0.19) duration of surgery (min): 234 vs 209 adequacy of oncological resection: margins (%): 11,9 vs 12,5 adequacy of oncological resection; lymph node removed: 9,7 vs 7,9

Characteristics of included studies (*Continued*)

	gastrointestinal recovery rate (days): 4,6 vs 7,2 hospital stay (days): 7,4 vs 11,9 (p=0.0001)
Notes	conversion (%): 21 follow-up: 55 months surgeons experience required: qualified surgeons in the Laparoscopic Colectomy for Cancer Trial. Retrospective review of laparoscopic and open APR was performed at three institutions. The decision to perform open or laparoscopic APR by the laparoscopic surgeon was not documented.
Allocation concealment	D – Not used

Study	**Goh 1997**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 20 vs 20 Gender (%): male 45 vs 30, female 55 vs 70 Inclusion: primary rectal cancer Exclusion: previous laparotomy, ultralow anterior resection Tumour stage UICC (%): I 15 vs 5, II 25 vs 25 , III 55 vs 55, IV 5 vs 15 Distance from anal verge (%):
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	morbidity (%): 20 vs 5 blood loss (ml): 50 vs 50 (p=n.s.) duration of surgery (min): 90 vs 73 (p=0.08) adequacy of oncological resection: margins (%): 0 vs 0 adequacy of oncological resection; lymph node removed: 20 vs 19 (p=0.44) gastrointestinal recovery rate (days): 3,5 vs 3,5 (p=n.s.) hospital stay (days): 5 vs 5,5 (p=0.13)
Notes	conversion (%): 0 follow-up: 8 vs 10 months surgeons experience required: no data given Patients without a palpable abdominal mass under anesthesia were subjected to laparoscopy and those with a palpable mass were subjected to an open resection.
Allocation concealment	D – Not used

Study	**Hartley 2001**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 21 vs 22 Gender (%): male 71 vs 68, female 29 vs 32 Inclusion: primary rectal cancer Exclusion: contraindication to laparoscopy (bowel obstruction or ascites) Tumour stage UICC (%): I 24 vs 18, II 48 vs 36, III 28 vs 46, IV 0 vs 0 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%): 71 vs 73 APR (%): 29 vs 27

Characteristics of included studies (*Continued*)

Outcomes	mortality (%): 0 vs 0 morbidity (%): 28,5 vs 18 anastomotic leakage (%): 19 vs 4,5 (p=0.32) local recurrence (%): 5 vs 4,5 (p=0.736) duration of surgery (min): 180 vs 125 (p=0.003) adequacy of oncological resection: margins (%): 0 vs 0 adequacy of oncological resection; lymph node removed: 6 vs 7 gastrointestinal recovery rate (days): 3 vs 4 hospital stay (days): 13,5 vs 15
Notes	conversion (%): 33 follow-up: 38 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Hu 2003**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 20 vs 25 Gender (%): male 45 vs 64, female 55 vs 36 Inclusion: primary rectal cancer Exclusion: age > 80 years or < 18 years, fixed palpable mass, T4 rectal cancer, metastatic disease, severe cardiovascular of respiratory dysfunction, previous abdominal operation, contraindication for pneumoperitoneum, malignancy within 5 years, synchronous adenocarcinoma, pregnancy, acute intestinal obstruction or perforation Tumour stage UICC (%):I 50 vs 24, II 20 vs 28, III 15 vs 28, IV 15 vs 20 Distance from anal verge (cm): 8,4 vs 7,0
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	mortality (%): 0 vs 0 morbidity (%): 0 vs 8 anastomotic leakage (%): 0 vs 4 local recurrence (%): 0 vs 0 duration of surgery (min): 227 vs 146 (p<0.05) gastrointestinal recovery rate (days): 3,2 vs 4,4 (p<0.05) hospital stay (days): 18,3 vs 18 (p=n.s.) immunologic response: no significant differences
Notes	conversion (%): 0 follow-up: 8 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Idani 1999**
Methods	Case-series (level of evidence 4)
Participants	n = 5 Gender (%): male 100 Inclusion: primary rectal cancer

Characteristics of included studies (*Continued*)

	Exclusion: no data given Tumour stage UICC (%): no data given Distance from anal verge (cm): 11,6
Interventions	only laparoscopy LAR (%): 100
Outcomes	mortality (%): 0 morbidity (%): 20 anastomotic leakage (%): 20 local recurrence (%): 0 blood loss (ml): 42 duration of surgery (min): 177 gastrointestinal recovery rate (days): 2,8 hospital stay (days): 16,2
Notes	conversion (%): no data given follow-up: 3 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Kockerling 2000**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 116 Gender (%): male 49, female 51 Inclusion: primary low rectal cancer Exclusion: no data given Tumour stage UICC (%): I 32.7, II 25.5, III 41.8, IV 0 Distance from anal verge (%): 4-6 cm= 29.3, 2-4 cm = 35.3, 0-2 cm= 32.8
Interventions	only laparoscopy APR (%): 100
Outcomes	overall survival rate at 3 years (%): 71.1 mortality (%): 1.7 morbidity (%): 34.4 reoperation (%): 5.2 local recurrence (%): 9.5 blood loss (ml): 436 duration of surgery (min): 226 adequacy of oncological resection; lymph node removed: 12.4 hospital stay (days): 21.6
Notes	conversion (%): 3.4 follow-up: 16 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Larach 1993**
Methods	Case-series (level of evidence 4)
Participants	n =4

Characteristics of included studies (*Continued*)

	Gender (%): no data given Inclusion: primary lower rectal cancer Exclusion: fistulization, large palpable mass, T4 rectal cancer Tumour stage UICC (%): I 0, II 50, III 50, IV 0 Distance from anal verge (%): no data given
Interventions	only laparoscopy APR (%): 100
Outcomes	mortality (%): 20 morbidity (%): 40 duration of surgery (min): 323 adequacy of oncological resection; lymph node removed: 4.75 gastrointestinal recovery rate (days): 4 hospital stay (days): 12.3
Notes	conversion (%): 20 follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Law 2004**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n =100 Gender (%): male 66, female 34 Inclusion: primary rectal cancer Exclusion: synchronous colon cancer, familial adenomatous polyposis Tumour stage UICC (%): 0 6, I 22, II 23, III 23, IV 11 Distance from anal verge: median level 10 cm
Interventions	only laparoscopic LAR (%): 92 APR (%): 8
Outcomes	mortality (%): 1 morbidity (%): 31 anastomotic leakage (%): 3 duration of surgery (min): 195 blood loss (ml): 200 incidence of blood transfusion (%): 6 gastrointestinal recovery rate (days): 3 hospital stay (days): 8
Notes	conversion (%): 15 follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Leroy 2004**
Methods	Individual cohort study

Characteristics of included studies (*Continued*)

	(level of evidence 2b) prospective
Participants	n = 102 Gender (%): male 56.1, female 43.9 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): CIS 7.1, I 22.4, II 29.6, III 33.7, IV 7.1 Distance from anal verge (%): 11-15 cm = 41.8, 6-10 cm = 35.7, 0-5 cm = 22.5
Interventions	only laparoscopy LAR (%): 86.7 APR (%): 13.3
Outcomes	5 -year disease-free survival rate (%): 75 mortality (%): 2 morbidity (%): 27 anastomotic leakage (%): 17 local recurrence (%): 6 duration of surgery (min): 202 adequacy of oncological resection; margins (%): 0 adequacy of oncological resection; lymph node removed: 8 gastrointestinal recovery rate (days): 4.1 hospital stay (days): 11.9
Notes	conversion (%): 3 follow-up: 36 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Leung 2000 a**
Methods	Individual RCT (level of evidence 1b) Prospective
Participants	n = 17 vs 17 Gender (%): male 35 vs 59, female 65 vs 41 Inclusion: primary rectal cancer Exclusion: distance from anal verge < 5 cm, tumour size > 6 cm, T4 rectal cancer, previous abdominal operations in lower pelvis, intestinal obstruction or perforation, metastatic disease, no informed consent Tumour stage UICC (%): I 0 vs 0, II 59 vs 53, III 41 vs 47, IV 0 vs 0 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	mortality (%): 0 vs 0 morbidity (%): 29 vs 35 duration of surgery (min): 212 vs 136 (p<0.001) blood loss (ml): 103 vs 141 (p=n.s.) incidence of blood transfusion (%): 6 vs 12 (p=n.s.) postoperative pain, pain score: 5.5 vs 6.25 (p=n.s.) postoperative pain, analgesia (no of injections): 3 vs 6 (p=n.s.) gastrointestinal recovery rate (days): 4 vs 4 (p=n.s.) hospital stay (days): 6 vs 7

	immunologic respons: Interleukin-1 (pg/ml): 0.28 vs 0.76 (p<0.05) Interleukin-6 (pg/ml): 57.38 vs 190.3 (p<0.05) C-reactive protein (mg/l): 65.3 vs 112.0 (p<0.05)
Notes	conversion (%): no data given follow-up: 22.6 vs 20.5 months surgeons experience required: no data given Rectosigmoid cancer was included.
Allocation concealment	D – Not used

Study	**Leung 2000 b**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 25 vs 34 Gender (%): male 60 vs 62, female 40 vs 38 Inclusion: primary rectal cancer Exclusion: bulky tumours, recurrent or metachronous disease Tumour stage UICC (%): I 4 vs 0, II 52 vs 35, III 20 vs 35, IV 24 vs 30 Distance from anal verge (cm): 4 vs 4.3
Interventions	laparoscopy vs open APR (%): 100
Outcomes	4-years disease-free survival rate (%): 84.2 vs 77.8 mortality (%): 0 vs 0 morbidity (%): 48 vs 62 local recurrence rate (%): 12 vs 15 duration of surgery (min): 215 vs 166 (p<0.001) blood loss (ml): 500 vs 1000 (p=0.02) adequacy of oncological resection; margins (%): 8 vs 3 (p=n.s.) adequacy of oncological resection; lymph node removed: 10 vs 12 (p=n.s.) postoperative pain: analgesia (no of injections): 5 vs 11 (p=0.02) gastrointestinal recovery rate (days): 4 vs 4 (p=0.04) hospital stay (days): 16 vs 25.5 (p=0.02)
Notes	conversion (%): 8 follow-up: 30.1 vs 28.3 months surgeons experience (years): 9 vs 9 The selection of patients for laparoscopy depended on the availability of informed consent, laparoscopic instruments, and surgeons experienced in laparoscopic surgery
Allocation concealment	D – Not used

Study	**Leung 2004 b**
Methods	Individual RCT (level of evidence 1b) Prospective
Participants	n = 203 vs 200 Gender (%):male 51 vs 49, female 49 vs 43 Inclusion: sigmoid and upper rectal cancer Exclusion:distance from anal verge < 5 cm, tumour size > 6 cm, T4 rectal cancer, previous abdominal operations in lower pelvis, intestinal obstruction or perforation, metastatic disease, no informed consent

Characteristics of included studies (*Continued*)

	Tumour stage UICC (%): I 15 vs 14, II 35 vs 37, III 32 vs 35, IV 18 vs 14 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	5-years disease-free survival rate (%): 75.3 vs 78.3 (p=0.45) mortality (%): 2 vs 1 morbidity (%): 19.7 vs 22.5 anastomotic leakage (%): 0.5 vs 2 local recurrence rate (%): 6.6 vs 4.1 duration of surgery (min): 190 vs 144 (p<0.001) blood loss (ml): 169 vs 238 (p=0.06) adequacy of oncological resection; lymph node removed: 11.1 vs 12.1 (p=0.18) postoperative pain, pain score: 4.6 vs 5.4 (p=0.003) postoperative pain, analgesia (no of injections): 4.5 vs 6.9 (p<0.001) gastrointestinal recovery rate (days): 4.2 vs 4.9 (p<0.001) hospital stay (days): 8.2 vs 8.7 (p<0.001) direct cost (US$): 9297 vs 7148
Notes	conversion (%): 23.2 follow-up: 52.7 vs 49.2 months surgeons experience required: all operations were done or directly supervised by surgeons skilled in both laparoscopic and colorectal surgery sample size calculation, randomisation preoperative, conversions analysed as intention to treat
Allocation concealment	B – Unclear

Study	**Lezoche 2002**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 42 vs 26 Gender (%): male 60 vs 53, female 40 vs 47 Inclusion: primary rectal cancer Exclusion: patients classified as T1N0 rectal cancer, who underwent local excision, high-risk ASA IV patients Tumour stage UICC (%): I 29.4 vs 19.2, II 35.3 vs 42.3, III 29.4 vs 34.6, IV 32 vs 25 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%): 71 vs 50 APR (%): 29 vs 50
Outcomes	4-years disease-free survival rate (%): 55.2 vs 50 (n.s.) mortality (%): 0 vs 0 local recurrence rate (%): 24.1 vs 25 (n.s.)
Notes	conversion (%): 19 follow-up: 49.4 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Morino 2003**
Methods	Individual cohort study

Characteristics of included studies (*Continued*)

	(level of evidence 2b) Prospective
Participants	n = 100 Gender (%): male 62, female 38 Inclusion: primary mid and low-rectal tumours Exclusion: specific contraindications to laparoscopy (severe cardiopulmonary disease, glaucoma), emergency surgery, intestinal occlusion, ASA I - III, T4 rectal cancer Tumour stage UICC (%): I 24, II 33, III 34, IV 9 Distance from anal verge (cm): 6.1
Interventions	only laparoscopy LAR (%): 100
Outcomes	5-years disease-free survival rate (%): 63 mortality (%): 2 morbidity (%): 36 anastomotic leakage (%): 17 local recurrence rate (%): 4.2 duration of surgery (min): 250 incidence of blood transfusions (%): 3 reoperation (%): 10 adequacy of oncological resection; margins (%): 0 adequacy of oncological resection; lymph node removed: 12.8 postoperative pain, analgesia: routinely, epidural local anesthetics (bupivacaine) were administered for 48 postoperative hours. Parenteral nonsteriodal analgesics (ketorolac) were required in 27 % of cases only up to postoperative day 2. gastrointestinal recovery rate (days): 3.3 hospital stay (days): 16.6
Notes	conversion (%): 12 follow-up: 45.7 months surgeons experience required: surgeons experienced in colorectal surgery and laparoscopic advanced surgery
Allocation concealment	D – Not used

Study	**Pasupathy 2001**
Methods	Individual case-control study (level of evidence 3b) Prospective
Participants	n = 11 vs 22 Gender (%): male 55 vs 50, female 45 vs 50 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 16 vs 19, II 52 vs 42, III 16 vs 28, IV 16 vs 11 Distance from anal verge (cm): 6 vs 7
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	mortality (%): 0 vs 0 morbidity (%): 18 vs 9 local recurrence rate (%): 0 vs 4 duration of surgery (min): 97.5 vs 90 (p=n.s.) postoperative pain, analgesia (days): 2 vs 3 (p<0.05) gastrointestinal recovery rate (days): 3 vs 3 (p=n.s.)

	hospital stay (days): 6.5 vs 6 (p=n.s.)
Notes	conversion (%): no data given follow-up: 12 months surgeons experience required: no data given. Groups were comparable for age, sex, tumour, anastomotic height from anal verge, stage of disease
Allocation concealment	D – Not used

Study	**Pietrabissa 2002**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 16 Gender (%): male 56, female 44 Inclusion: primary rectal cancer with lowest edge located between 3 and 12 cm from the anal verge Exclusion: previous extensive abdominal surgery, T4 rectal cancer Tumour stage UICC (%): I 0, II 50, III 31, IV 29 Distance from anal verge (cm): 6.4
Interventions	only laparoscopy LAR (%): 100
Outcomes	mortality (%): 0 morbidity (%): 19 anastomotic leakage (%): 0 duration of surgery (min): 233 postoperative pain, analgesia: 10 patients were off pain medication on postoperative day 3, with occasional use of analgetics reported by the remaining 6 patients. hospital stay (days): 6.6
Notes	conversion (%): 0 follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Poulin 2002**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 80 Gender (%): male 63, female 37 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 16, II 35, III 36, IV 13 Distance from anal verge (%): 12-15 cm = 38, 8-11 cm = 20, 0-7 cm = 42
Interventions	only laparoscopy LAR (%): 65 APR (%): 35
Outcomes	overall 5-years survival rate (%): 72.1 mortality (%): 2.5 morbidity (%): 40

	anastomotic leakage (%): 5.7 local recurrence rate (%): 3.75 duration of surgery (min): LAR 200, APR 215 hospital stay (days): LAR: 6.5, APR 8
Notes	conversion (%): 18.25 follow-up: 31 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Ramos 1997**
Methods	Individual case-control study (level of evidence 3b) Prospective
Participants	n = 18 vs 18 Gender (%): male 33 vs 55 , female 67 vs 45 Inclusion: low rectal cancer Exclusion: no data given Tumour stage UICC (%): I 17 vs 11, II 17 vs 28, III 55 vs 55, IV 11 vs 6 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open APR (%): 100
Outcomes	mortality (%): 0 vs 5.5 morbidity (%): 44 vs 66 reoperation (%): 0 vs 11 local recurrence (%): 6 vs 17 (p=0.28) duration of surgery (min): 229 vs 208 (p=0.47) adequacy of oncological resection: lymph nodes removed: 11.1 vs 7.8 (p=0.30) postoperative pain, analgesia (days): 2.2 vs 3.2 (p<0.005) gastrointestinal recovery rate (days): 2.5 vs 3.8 (p< 0.005) hospital stay (days): 7.4 vs 12.9 (p< 0.005)
Notes	conversion (%): 10 follow-up: 20 months surgeons experience required: the same surgical team performed the operations on both groups of patients. The availability of operating room laparoscopic equipment determined the type of operation (laparoscopic or open)
Allocation concealment	D – Not used

Study	**Reis Neto 2002**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 32 Gender (%): male 50, female 50 Inclusion: low rectal cancer, distal marge 4 cm from the pectinate line Exclusion: T4 rectal cancer Tumour stage, T-classification (%): I 3.2, II 71.8, III 25, IV 0 Distance from anal verge (%): no data given

Characteristics of included studies (*Continued*)

Interventions	only laparoscopy LAR (%): 100
Outcomes	local recurrence (%): 3.12 adequacy of oncological resection: lymph nodes removed: 12.3 hospital stay (days): 5.12
Notes	conversion (%): 3.1 follow-up: 14 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Rullier 2003**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 32 Gender (%): male 65, female 35 Inclusion: mid or low rectal cancer (lower edge less than 12 cm from anal verge) Exclusion: T4 rectal cancer, synchronous metastates, coexisting colon pathology, previous local excision for T3, ventriculoperitoneal valve, teaching cases. Tumour stage UICC (%): I 3, II 13, III 81, IV 3 Distance from anal verge (cm): 5
Interventions	only laparoscopy LAR (%): 100
Outcomes	mortality (%): 3 morbidity (%): 31 anastomotic leakage (%): 0 local recurrence (%): 0 duration of surgery (min): 420 incidence of blood transfusions (%): 18 adequacy of oncological resection: margin (%): 6 adequacy of oncological resection: lymph nodes removed: 10 hospital stay (days): 9
Notes	conversion (%): 9 follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Scheidbach 2002**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 308 Gender (%): male 48, female 52 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 33.9, II 29.4, III 36.7 Distance from anal verge (%): no data given

Characteristics of included studies (*Continued*)

Interventions	only laparoscopy LAR (%): 60.8 APR (%): 39.2
Outcomes	2-years disease free survival rate: APR 62.4, LAR 54.8 mortality (%): 1.6 morbidity (%): 37.6 anastomotic leakage (%): 13.9 reoperation(%): 7.4 local recurrence rate (%): 6.6 duration of surgery (min): 208 adequacy of oncological resection: lymph nodes removed: 13.0
Notes	conversion (%): 6.1 follow-up: 24.8 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Schiedeck 2000**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 259 Gender (%): male 92, female 8 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 35, II 7, III 58, IV 0 Distance from anal verge (%): no data given
Interventions	only laparoscopy LAR (%): 60.6 APR (%): 39.4
Outcomes	mortality (%): LAR 0, APR 2 morbidity (%): LAR 26.4, APR 44.2 anastomotic leakage (%): 3.9 reoperation(%): LAR 6.4, APR 15.7 local recurrence rate (%): LAR 1.9, APR 2.9 duration of surgery (min): LAR 235, APR 257 postoperative pain, analgetics (days): no use of analgetics on day 6 adequacy of oncological resection: lymph nodes removed: 12.1 gastrointestinal recovery (days): LAR 4.3, APR 4.9 hospital stay (days): 14.4
Notes	conversion (%): 6.6 follow-up (months): LAR 26, APR 32 surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Schwander 1999**
Methods	Individual case-control study (level of evidence 3b) Prospective

Characteristics of included studies (*Continued*)

Participants	n = 32 vs 32 Gender (%): male 65 vs 56 , female 35 vs 44 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 59, II 3, III 38, IV 0 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%):59.3 APR (%): 40.7
Outcomes	3-year survival rate (%): 93 vs 93 morbidity (%): 31.3 vs 31.3 anastomotic leakage (%): 0 vs 3.1 local recurrence rate (%): 3.1 vs 0 duration of surgery (min): 281 vs 209 (p=0.0004) blood transfusions (U): 1.2 vs 2.4 (p= 0.017) postoperative pain, analgetics (days): 3.3 vs 3.6 (p=0.7) adequacy of oncological resection: margins: 0 vs 0 adequacy of oncological resection: lymph nodes removed: 12.9 vs 13.0 (p=0.5) gastrointestinal recovery (days): 4.3 vs 5.8 (p=0.0002) hospital stay (days): 15.3 vs 21.9 (p=0.052)
Notes	conversion (%): 0 follow-up: 32 months surgeons experience required: no data given The two groups were matched for age, UICC stage, tumour site, type of resection.
Allocation concealment	D – Not used

Study	**Seow-Choen 1997**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 16 vs 11 Gender (%): male 50 vs 64, female 50 vs 36 Inclusion: primary low rectal cancer Exclusion: no data given Tumour stage UICC (%): I 31 vs 36, II 37 vs 28, III 25 v 36, IV 7 vs 0 Distance from anal verge (cm): 2 vs 3 (p=0.13)
Interventions	laparoscopy vs open APR (%): 100
Outcomes	mortality (%): 0 vs 0 local recurrence rate (%): 0 vs 0 duration of surgery (min): 110 vs 100 (p=0.43) blood loss (ml): 200 vs 100 (p=0.35) postoperative pain, analgetics (days): 2 vs 3 (p=0.10) adequacy of oncological resection: margins (%): 0 vs 0 adequacy of oncological resection: lymph nodes removed: 10 vs 10 gastrointestinal recovery (days): 3 vs 4 (p=0.005)

Characteristics of included studies (*Continued*)

	hospital stay (days): 6.5 vs 8 (p=0.0057)
Notes	conversion (%): no data given follow-up (months): 12 vs 33 surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Tate 1993**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 11 vs 14 Gender (%): male 45 vs 43, female 55 vs 57 Inclusion: proximal rectal cancer Exclusion: distal rectal tumour (anastomosis < 5 cm of the dentate line), fixed mass palpable, previous radiotherapy or extensive abdominal surgery, age > 65 years, metastatic disease not treatable by surgery Tumour stage UICC (%): I 9 vs 0, II 37 vs 64, III 45 vs 36, IV 0 vs 0 Distance from anal verge (cm): 20 vs 15
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	morbidity (%): 45 vs 29 duration of surgery (min): 205 vs 123 (p=0.01) postoperative pain, analgetics (days): 2.6 vs 7.4 (p=0.011) adequacy of oncological resection: lymph nodes removed: 10 vs 13 gastrointestinal recovery (days): 2.5 vs 3.6 (p=0.008) hospital stay (days): 12.3 vs 14.3 (p=0.08)
Notes	conversion (%): no data given follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Tsang 2003**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 44 Gender (%): male 48, female 52 Inclusion: primary rectal cancer with lower margin < 10 cm from anal verge Exclusion: distant metastasis, T4 rectal cancer, patient considered unfit for major operation Tumour stage UICC (%): I 23, II 25, III 52, IV 0 Distance from anal verge (cm): 4
Interventions	only laparoscopy LAR (%): 100
Outcomes	2-years disease free survival rate (%): 68 mortality (%): 0 morbidity (%): 38.6 anastomotic leakage (%): 0 reoperation (%): 9

Characteristics of included studies (*Continued*)

	local recurrence rate (%): 4.5 duration of surgery (min): 180 blood loss (ml): 80 adequacy of oncological resection: margins (%): 2 gastrointestinal recovery (days): 2 hospital stay (days): 8
Notes	conversion (%): 0 follow-up (months): 15 surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Vithiananthan 2001**
Methods	Case-series (level of evidence 4) Retrospective
Participants	n = 27 vs 17 Gender (%): male 80 vs 11, female 20 vs 56 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): no data given Distance from anal verge (cm): 9.5 vs 9.6 (p=0.9)
Interventions	laparoscopy vs open LAR (%): 100
Outcomes	mortality (%): 0 vs 0 morbidity (%): 26 vs 28 (p>0.05) anastomotic leakage (%): 3 vs 10 (p>0.05) adequacy of oncological resection; lymph nodes removed: 12 vs 11 (p=0.81) gastrointestinal recovery (days): 5 vs 6.2 (p=0.07) hospital stay (days): 6.1 vs 11.1 (p=0.0006)
Notes	conversion (%): no data given follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Watanabe 2000**
Methods	Case-series (level of evidence 4)
Participants	n = 7 Gender (%): male 43, female 57 Inclusion: primary rectal cancer, tumour location < 5 cm of dentate line Exclusion: no data given Tumour stage UICC (%): I 71, II 29, III 0, IV 0 Distance from anal verge (%): no data given
Interventions	only laparoscopy LAR (%): 100
Outcomes	mortality (%): 0 reoperation (%): 0 anastomotic leakage (%):14

Characteristics of included studies (*Continued*)

	duration of surgery (min): 280-450
Notes	conversion (%): no data given follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Weiser 2000**
Methods	Case-series (level of evidence 4)
Participants	n = 21 Gender (%): no data given Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): no data given Distance from anal verge (%): no data given
Interventions	only laparoscopy LAR (%): no data given APR (%): no data given
Outcomes	local recurrence (%): 0 duration of surgery (min); 300 blood loss (ml): 225 hospital stay (days): 6
Notes	conversion (%): no data given follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Wu 1997**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 14 Gender (%): no data given Inclusion: rectal cancer Exclusion: no data given Tumour stage UICC (%): I and II 36, III 50, IV 14 Distance from anal verge (%): no data given
Interventions	only laparoscopy APR (%): 100
Outcomes	morbidity (%): 42 local recurrence (%): 7 duration of surgery (min): 240 blood loss (ml): 418 blood transfusions (%): 25 postoperative pain, analgesia (days): 2 gastrointestinal recovery (days): 4

Characteristics of included studies (*Continued*)

Notes	conversion (%): 14 follow-up: 17 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Wu 2004**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 18 vs 18 Gender (%): male 50 vs 55, female 50 vs 45 Inclusion: primary rectal cancer Exclusion: no data given Tumour stage UICC (%): I 17 vs 17, II 50 vs 39, III 33 vs 44, IV 0 vs 0 Distance from anal verge (%): no data given
Interventions	laparoscopy vs open LAR (%): 61vs 66 APR (%): 39 vs 34
Outcomes	morbidity (%): 5.6 vs 27.8 (p<0.05) anastomotic leakage (%): 0 vs 0 duration of surgery (min): 189 vs 146 (p<0.05) blood loss (ml): 136 vs 357 (p<0.01) adequacy of oncological resection: margins (%): 0 vs 0 adequacy of oncological resection; lymph nodes removed: 7.8 vs 8.2 (p=n.s.) gastrointestinal recovery (days): 2.4 vs 3.7 (p<0.05) hospital stay (days): 7.8 vs 9.1 (p=n.s.)
Notes	conversion (%): 0 follow-up: no data given surgeons experience required: experienced in advanced laparoscopic techniques
Allocation concealment	D – Not used

Study	**Yamamoto 2002**
Methods	Case-series (level of evidence 4) Prospective
Participants	n = 70 Gender (%): male 57, female 43 Inclusion: primary rectal carcinoma Exclusion: T3 or T4 rectal cancer Tumour stage UICC (%): I 12.9, II 60, III 12.9, IV 1.4 Distance from anal verge (%): 12.1 -17 cm = 47, 7.1-12 cm = 26, 0-7 cm = 27
Interventions	only laparoscopy LAR (%): 94.3 APR (%): 5.7
Outcomes	5-years disease-free survival rate (%): 92.1 mortality (%): 0 morbidity (%): 18.6

Characteristics of included studies (*Continued*)

	local recurrence (%): 2.8 anastomotic leakage (%): 8.6 reoperation (%): 8.6 adequacy of oncological resection: margins (%): 0 adequacy of oncological resection; lymph nodes removed: 14.3 gastrointestinal recovery (days): 3 hospital stay (days): 8
Notes	conversion (%): 2.9 follow-up: 23 months surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Yamamoto 2005**
Methods	Individual cohort study (level of evidence 2b) Prospective
Participants	n = 31 Gender (%): male 58, female 42 Inclusion: primary rectal cancer Exclusion: tumour size > 6 cm, history of extensive adhesions, BMI > 32 kg/m2, intestinal obstruction, refusal to undergo laparoscopy, T3 and T4 rectal cancer in middle and lower rectum, tumours 0-2 cm from anal verge Tumour stage UICC (%): I 75, II 0, III 19, IV 6 Distance from anal verge (%): 12,1-17 cm = 21, < 12 cm 10
Interventions	only laparoscopic LAR (%):100
Outcomes	duration of surgery (min): 267 blood loss (ml): 56 gastrointestinal recovery rate (days): 3 hospital stay (days): 8
Notes	conversion (%): 0 follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Study	**Zhou 2004**
Methods	Individual RCT (level of evidence 1b) Prospective
Participants	n= 82 vs 89 Gender (%): male 56 vs 48, female 44 vs 52 Inclusion: primary rectal cancer with lowest margin of tumour located under the peritoneal reflection and 1.5 cm above the dentate line Exclusion: rectal cancer of other pathological type (e.g. lymphoma), emergency surgery, Dukes D tumours with local infiltration affecting adjecent organs, patients unwilling to take part in the study Tumour stage UICC (%): I 6 vs 7, II 12 vs 9, III 77 vs 76, IV 5 vs 8 Distance from dentate line (%): 1.5 - 4 cm = 59 vs 63, 4.1- 7 cm = 41 vs 37

Interventions	laparoscopy vs open LAR (%): 100
Outcomes	mortality (%): 0 vs 0 morbidity (%): 6.1 vs 12.4 (p=0.016) anastomotic leakage (%): 1.2 vs 3.4 duration of surgery (min): 120 vs 106 (p=0.051) blood loss (ml): 20 vs 106 (p=0.025) postoperative pain, analgesia (days): 3.9 vs 4.1 (p=0.225) gastrointestinal recovery (days): 4.3 vs 4.5 (p=0.368) hospital stay (days): 8.1 vs 13.3 (p=0.001)
Notes	conversion (%): no data given follow-up: no data given surgeons experience required: no data given
Allocation concealment	D – Not used

Characteristics of excluded studies

Study	Reason for exclusion
Barlehner 1998	patients and data are included in Barlehner 2005
Bohm 1999	primary outcome of laparoscopic TME unknown
Braga 2002	primary outcome of laparoscopic TME unknown
Decanini 1994	cadaver study, no primary rectal cancer was diagnosed
Fleshman JW	primary outcome of laparoscopic TME unknown
Hartley 2000	primary outcome of laparoscopic TME unknown
Iroatulam 1998	primary outcome of laparoscopic TME unknown. Different diagnoses were described (i.e. adenocarcinoma and melanoma and leiomyosarcoma and squamous cell carcinoma)
Kessler 2005	case-report; only one patient is described
Kockerling 1998	primary outcome of laparoscopic TME unknown
Kockerling 1999	primary outcome of laparoscopic TME unknown
Leung 1997	patients and data are included in Leung 2004b
Leung 1999	Patients and data are included in Leung 2004b
Leung 2004	primary outcome of laparoscopic TME unknown
Lord 1996	primary outcome of laparoscopic TME unknown
Milsom 1998	primary outcome of laparoscopic TME unknown
Moloo 2004	primary outcome of laparoscopic TME unknown
Parise 2004	primary outcome of laparoscopic TME unknown
Patankar 2003	primary outcome of laparoscopic TME unknown
Poulin 1999	primary outcome of laparoscopic TME unknown
Poulin 2001	primary outcome of laparoscopic TME unknown
Rhodes 1996	primary outcome of laparoscopic TME unknown
Rose 2004	primary outcome of laparoscopic TME unknown
Scheidbach 2001	patients and data are included in Scheidbach 2002
Schwenk 1998	primary outcome of laparoscopic TME unknown

Characteristics of excluded studies (*Continued*)

Schwenk 1998-2	primary outcome of laparoscopic TME unknown
Schwenk 1999	primary outcome of laparoscopic TME unknown
Schwenk 2000	primary outcome of laparoscopic TME unknown
Slim 1994	primary outcome of laparoscopic TME unknown
Stead 2000	primary outcome of laparoscopic TME unknown
Vignali 2004	primary outcome of laparoscopic TME unknown
Wichmann 2005	primary outcome of laparoscopic TME unknown
Zhou 2003	patients and data are included in Zhou 2004

GRAPHS AND OTHER TABLES

This review has no analyses.

INDEX TERMS

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COVER SHEET

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